OBSTETRICS

Effect of delayed cord clamping on very preterm infants

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OBJECTIVE: Despite significant proposed benefits, delayed umbilical cord clamping (DCC) is not practiced widely in preterm infants largely because of the question of feasibility of the procedure and uncertainty regarding the magnitude of the reported benefits, especially intraventricular hemorrhage (IVH) vs the adverse consequences of delaying the neonatal resuscitation. The objective of this study was to determine whether implementation of the protocol-driven DCC process in our institution would reduce the incidence of IVH in very preterm infants without adverse consequences.

STUDY DESIGN: We implemented a quality improvement process for DCC the started in August 2013 in infants born at ≤32 weeks' gestational age. Eligible infants were left attached to the placenta for 45 seconds after birth. Neonatal process and outcome data were collected until discharge. We compared infants who received DCC who were born between August 2013 and August 2014 with a historic cohort of infants who were born between August 2012 and August 2013, who were eligible to receive DCC, but whose cord was clamped immediately after birth, because they were born before the protocol implementation.

RESULTS: DCC was performed on all the 60 eligible infants; 88 infants were identified as historic control subjects. Gestational age, birthweight, and other demographic variables were similar between both groups. There were no differences in Apgar scores or admission temperature, but significantly fewer infants in the DCC cohort were intubated in delivery room, had respiratory distress syndrome, or received red blood cell transfusions in the first week of life compared with the historic cohort. A significant reduction was noted in the incidence of IVH in the DCC cohort compared with the historic control group (18.3% vs 35.2%). After adjustment for gestational age, an association was found between the incidence of IVH and DCC with IVH was significantly lower in the DCC cohort compared with the historic cohort; an odds ratio of 0.36 (95% confidence interval, 0.15—0.84; $P < .05$). There were no significant differences in deaths and other major morbidities.

CONCLUSION: DCC, as performed in our institution, was associated with significant reduction in IVH and early red blood cell transfusions. DCC in very preterm infants appears to be safe, feasible, and effective with no adverse consequences.

Key words: delaying umbilical cord clamping, intraventricular hemorrhage, very preterm infant

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There is growing evidence that enhanced placental transfusion by delaying umbilical cord clamping (DCC) in very preterm infants may improve hemodynamic stability after birth and decrease the incidence of major neonatal morbidities, such as intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC).[1-6] Recently, the American College of Obstetricians and Gynecologists (ACOG) published a committee opinion that supported DCC in preterm infants, with the possibility for a nearly 50% reduction in IVH.[7] However, the practice of DCC in preterm infants has not been adopted widely, mainly because of the concern of a delay in initiating resuscitation in this vulnerable population.[8] Furthermore, there is uncertainty regarding the magnitude of published benefits in very preterm infants because previous trials were limited by small sample sizes, wide variability in the technique, and inconsistent reporting of factors that may have contributed to clinical outcomes.[9,10]

We recently implemented a DCC quality improvement (QI) process in very preterm infants at a large delivery hospital. The objective of this cohort study was to evaluate the clinical consequences of a protocol-driven DCC implementation in singleton infants who were born at ≤32 weeks' gestation. We hypothesized that DCC would not compromise initial resuscitation and

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would be associated with a significant decrease in early red blood cell transfusions and IVH compared with a historic cohort.

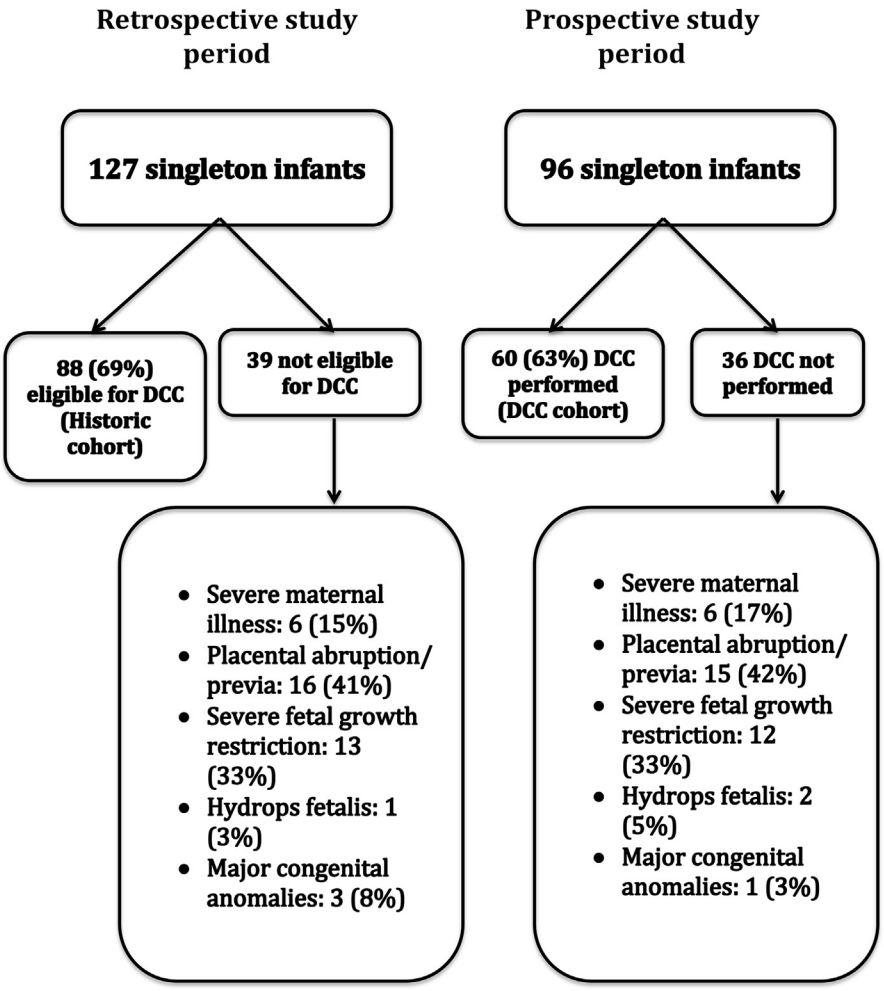
Materials and Methods

On average, our level III Neonatal Intensive Care Unit cares for approximately 200 very preterm inborn infants every year. The previous routine clinical practice was to clamp the umbilical cord immediately after the birth. The DCC QI process was implemented starting August 2013. All infants born at ≤32 weeks' gestation were eligible for DCC, unless they met the following exclusion criteria: severe maternal illness that prompted immediate delivery, placental causes (abruption or previa) or fetal causes (multiple gestation, major congenital anomalies, severe growth restriction, or hydrops fetalis). After birth, the infant was left unstimulated, attached at or slightly below the level of placenta for 45 seconds. The cord was then clamped and cut, and the neonatal team initiated resuscitation efforts. Apgar timing was initiated at the time of birth when the infant was delivered completely.

With approval by the institutional review board, prospective and retrospective data were extracted from maternal and neonatal electronic medical records. The prospective study period was 1 year, from Aug.19, 2013, to Aug. 18, 2014. The study period for the historic cohort was also 1 year, from Aug. 19, 2012, to Aug. 18, 2013. Collected data included maternal demographics, obstetric complications, any antenatal steroid and magnesium use, and other labor and delivery variables. Neonatal data included gestational age, birthweight, sex, postdelivery data variables such as Apgar scores, resuscitation data, and the infant's temperature upon admission to the neonatal intensive care unit. Other clinical variables included treatment with phototherapy, (*intensive phototherapy* defined as irradiance in the blue-green spectrum of at least 30 μW/cm^2 per nm),[11] red blood cell transfusions, and inotropic and corticosteroid therapy within 1 week of life. Additional outcome variables included incidence of respiratory distress syndrome (RDS), surfactant therapy, therapy for patent ductus arteriosus, and incidence of culture positive sepsis. We also recorded major outcomes such as death, bronchopulmonary dysplasia (BPD), NEC Bell's stage ≥2,[12] retinopathy of prematurity (ROP), and IVH. Diagnosis of BPD was made at 36 weeks postmenstrual age if there was any oxygen requirement.[13] Any operative interventions for NEC or ROP were also documented.[14] IVH was graded 1-4 based on the criteria developed by Papile et al[15] who defined *grades 3* and *4* as severe IVH. White matter injury such as periventricular leukomalacia and porencephaly also were documented.

All statistical analysis was performed with SAS Enterprise Guide software (version 5.1; SAS Institute Inc, Cary, NC). Demographic and outcome variables were compared between the DCC cohort and historic control groups with the use of the Student *t* test for continuous variables, and χ^2 or Fisher exact test for categoric variables. We also calculated odds ratios (with 95% confidence interval) for comparisons after adjustment for gestation. Death and

FIGURE
Distribution of the cohorts



During the retrospective study period, 88 (69%) singleton infants were eligible to receive DCC (historic cohort). During the prospective study period, 60 (63%) singleton infants received DCC (DCC cohort). Different exclusion criteria are shown in the figure.

DCC, delaying umbilical cord clamping.

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